CLAIMS

What is claimed is:

1. A synthetic oligonucleotide comprising at least seven nucleotides or nucleotide analogues having a sequence corresponding to the entire untranslated 3′ region (3′-UTR) of mRNA of a housekeeping gene or a consecutive sequence segment of said 3′-UTR.

2. The synthetic oligonucleotide as set forth in claim 1 wherein the housekeeping gene is a gene encoding a protein regulating DNA synthesis and repair.

3. The synthetic oligonucleotide as set forth in claim 2 wherein the housekeeping gene is a gene encoding proteins involved in purine and pyrimidine synthesis.

4. The synthetic oligonucleotide as set forth in claim 1 wherein said segment is selected to have a reduced dimer formation, reduced self-complementary interactions and reduced binding potential to the UTR sequence.

5. The synthetic oligonucleotide as set forth in claim 1 wherein the housekeeping gene encodes ribonucleotide reductase dimeric protein components designated R1 and R2.

6. The synthetic oligonucleotide as set forth in claim 5 wherein the oligonucleotide has a sequence corresponding to the entire 3′-UTR of the mRNA for the R1 component (SEQ ID No:1) or segment thereof substantially free of the coding sequence of ribonucleotide reductase protein R1.

7. The synthetic oligonucleotide as set forth in claim 6 wherein the oligonucleotide segment has a sequence as set forth in Table 4.

8. The synthetic oligonucleotide as set forth in claim 6 wherein the oligonucleotide segment has a sequence as set forth in SEQ ID No:45.

9. The synthetic oligonucleotide as set forth in claim 5 wherein the oligonucleotide has a sequence corresponding to the entire 3'-UTR of the mRNA for the R2 component (SEQ ID No:2) or segment thereof substantially free of the coding sequence of ribonucleotide reductase protein R2.

10. The synthetic oligonucleotide as set forth in claim 9 wherein the oligonucleotide segment has a sequence as set forth in Table 5.

11. The synthetic oligonucleotide as set forth in claim 9 wherein the oligonucleotide segment has a sequence as set forth in SEQ ID Nos:6-12.

12. A pharmaceutical composition for inhibiting the tumorigenicity of neoplastic cells in a mammal consisting of

an effective amount of at least one active ingredient as set forth in claim 1 and a pharmaceutically physiologically acceptable carrier or diluent.

13. A pharmaceutical composition for modulating tumorigenicity of neoplastic cells in a mammal consisting of

an effective amount of at least one active ingredient as set forth in claim 6 or the antisense sequence thereof or a ribozyme comprising a sequence complementary to at least a portion of said UTR; and

a pharmaceutically physiologically acceptable carrier or diluent.

14. A pharmaceutical composition for modulating tumorigenicity of neoplastic cells in a mammal consisting of

an effective amount of at least one active ingredient as set forth in claim 9 or the antisense sequence thereof or a ribozyme comprising a sequence complementary to at least a portion of said UTR; and

a pharmaceutically physiologically acceptable carrier or diluent.

15. A pharmaceutical composition for inhibiting metastasis of a neoplastic cell in a mammal consisting of

an effective amount of at least one active ingredient as set forth in claim 9 or the antisense sequence thereof or a ribozyme comprising a sequence complementary to at least a portion of said UTR; and

a pharmaceutically physiologically acceptable carrier or diluent.

16. A pharmaceutical composition for modulating tumorigenicity of a neoplastic cell in a mammal consisting of

an effective amount of at least two active ingredients selected from oligonucleotides having a sequence corresponding to the entire 3'-UTR of the mRNA for the R1 or R2 component or sequence segments of at least seven consecutive nucleotides thereof substantially free of the coding sequence of ribonucleotide reductase protein R1 or R2 respectively or the antisense sequences thereof or ribozymes comprising a sequence complementary to at least a portion of said UTR; and

a pharmaceutically physiologically acceptable carrier or diluent.

17. The pharmaceutical composition as set forth in claim 16 wherein said sequence segment is selected to have a reduced dimer formation, reduced self-complementary interactions and reduced binding potential to the UTR sequence.

18. A method of modulating the tumorigenicity of neoplastic cells in a mammal by

contacting said neoplastic cell with a growth inhibiting amount of at least one oligonucleotide having a sequence of at least seven consecutive nucleotides or nucleotide analogues of a 3′ untranslated region (3′-UTR) of mRNA of a housekeeping gene of the mammal substantially free of the coding sequence of the housekeeping gene.

19. The method as set forth in claim 18 wherein said sequence segment is selected to have a reduced dimer formation, reduced self-complementary interactions and reduced binding potential to the UTR sequence.

20. The method as set forth in claim 18 wherein the housekeeping gene is a gene encoding a protein regulating DNA synthesis and repair.

21. The method as set forth in claim 20 wherein the housekeeping gene is a gene encoding proteins involved in purine and pyrimidine synthesis.

22. The method as set forth in claim 20 wherein the housekeeping gene encodes ribonucleotide reductase dimeric protein components designated R1 and R2.

23. The method as set forth in claim 22 wherein the oligonucleotide has a sequence corresponding to the entire 3′-UTR of the mRNA for the R1 component or segment thereof substantially free of the coding sequence of ribonucleotide reductase protein R1.

24. The method as set forth in claim 23 wherein the oligonucleotide segment has a sequence as set forth in Table 4.

25. The method as set forth in claim 24 wherein the oligonucleotide segment has a sequence as set forth in SEQ ID No:45.

26. The method as set forth in claim 22 wherein the oligonucleotide has a sequence corresponding to the entire 3'-UTR of the mRNA for the R2 component or segment thereof substantially free of the coding sequence of ribonucleotide reductase protein R2.

27. The method as set forth in claim 26 wherein the oligonucleotide segment has a sequence as set forth in Table 5.

28. The method as set forth in claim 27 wherein the oligonucleotide has a sequence as set forth in SEQ ID Nos:6-12.

29. A method of modulating the tumorigenicity of neoplastic cells in a mammal by

contacting said neoplastic cell with a growth inhibiting amount of at least two active compositions from oligonucleotides having a sequence corresponding to the entire 3'-UTR of the mRNA for the R1 or R2 component or sequence segments of at least seven consecutive nucleotides thereof substantially free of the coding sequence of ribonucleotide reductase protein R1 or R2 respectively or the antisense sequences thereof or ribozymes comprising a sequence complementary to at least a portion of the UTR.

30. A synthetic oligonucleotide as set forth in claim 1 comprising at least two sequences of a consecutive

segment of an untranslated 3′ region (3′-UTR) of mRNA of a housekeeping gene linked together.

31. A method of inhibiting the tumorigenicity of neoplastic cells resistant to hydroxyurea in a mammal by

identifying patients who have tumors that are resistant to hydroxyurea and

contacting the tumor with a growth inhibiting amount of at least one active composition from oligonucleotides having a sequence corresponding to the entire 3′-UTR of the mRNA for the R1 or R2 component or segments thereof substantially free of the coding sequence of ribonucleotide reductase protein R1 or R2 respectively or the antisense sequences thereof or ribozymes comprising a sequence complementary to at least a portion of the UTR.

32 ~~33~~. An antibody directed against the oligonucleotides selected from the group having a sequence corresponding to the entire 3′-UTR of the mRNA for the R1 or R2 component or segments thereof substantially free of the coding sequence of ribonucleotide reductase protein R1 or R2 respectively.

33 ~~34~~. A method for identifying a substance that modulates the tumorigenic properties of a cell comprising:

(a) reacting a test substance with an oligonucleotide comprising at least seven consecutive nucleotides or nucleotide analogues of an untranslated region of mRNA of a housekeeping gene, under conditions which permit the formation of complexes between the test substance and oligonucleotide; and

(b) assaying for complexes, for free substance, for non-complexed oligonucleotide to determine if the substance binds to the oligonucleotide and thereby modulates tumorigenic properties of a cell.

34 ~~35~~. A method for screening for an agonist or antagonist of the interaction of an oligonucleotide with a

substance which binds to the oligonucleotide, wherein the oligonucleotide comprises at least seven consecutive nucleotides or nucleotide analogues of an untranslated region of mRNA of a housekeeping gene and thereby modulates the tumorigenic properties of a cell comprising:

(a) providing a known concentration of the oligonucleotide and a substance which is capable of binding to the oligonucleotide, and a test substance under conditions which permit the formation of complexes between the substance and oligonucleotide; and

(b) assaying for complexes, for free substance, for non-complexed oligonucleotide to determine if the substance is an agonist or antagonist of the interaction of the substance and oligonucleotide, and thereby modulates tumorigenic properties of a cell.